Lasers in Surgery and Medicine 23:94–103 (1998)

In Situ Temperature Measurements With Thermocouple Probes During Laser Interstitial Thermotherapy (LITT): Quantification and Correction of a Measurement Artifact

Fabrice Manns, PhD,[1,2]* Peter J. Milne, PhD,[2,3] Xochitl Gonzalez-Cirre, MS,[1,2] David B. Denham, MS,[1,2] Jean-Marie Parel, PhD,[1,3] and David S. Robinson, MD[4]

[1]Department of Biomedical Engineering, University of Miami College of Engineering, Coral Gables, Florida 33146
[2]Ophthalmic Biophysics Center, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida 33146
[3]Division of Marine and Atmospheric Chemistry, University of Miami Rosenstiel School of Marine and Atmospheric Sciences, Key Biscayne, Florida 33149
[4]Sylvester Comprehensive Cancer Center, University of Miami School of Medicine, Miami, Florida 33136

Background and Objective: **The purpose of this work was to quantify the magnitude of an artifact induced by stainless steel thermocouple probes in temperature measurements made in situ during experimental laser interstitial thermo-therapy (LITT). A procedure for correction of this observational error is outlined.**
Study Design/Materials and Methods: **A CW Nd:YAG laser system emitting 20W for 25–30 s delivered through a fiber-optic probe was used to create localized heating. The temperature field around the fiber-optic probe during laser irradiation was measured every 0.3 s in air, water, 0.4% intralipid solution, and fatty cadaver pig tissue, with a field of up to fifteen needle thermocouple probes.**
Results: **Direct absorption of Nd:YAG laser radiation by the thermocouple probes induced an overestimation of the temperature, ranging from 1.8°C to 118.6°C in air, 2.2°C to 9.9°C in water, 0.7°C to 4.7°C in intralipid and 0.3°C to 17.9°C in porcine tissue after irradiation at 20W for 30 s and depending on the thermocouple location. The artifact in porcine tissue was removed by applying exponential and linear fits to the measured temperature curves.**
Conclusion: **Light absorption by thermocouple probes can induce a significant artifact in the measurement of laser-induced temperature increases. When the time constant of the thermocouple effect is much smaller than the thermal relaxation time of the surrounding tissue, the artifact can be accurately quantified. During LITT experiments where temperature differences of a few degrees are significant, the thermocouple artifact must be removed in order to be able accurately to predict the treatment outcome. Lasers Surg. Med. 23:94–103, 1998.**

Key words: breast cancer; hyperthermia; laser-tissue interaction; tissue temperature measurements

Contract grant sponsor: Department of Defense Breast Cancer Research Program; Contract grant number: DAMD 17-94-J-4246; Contract grant sponsor: Kemper Foundation, Kansas City, MO.

*Correspondence to: Fabrice Manns, University of Miami, 1638 NW 10th Avenue, Miami, FL 33136.

Accepted 11 May 1998

INTRODUCTION

Laser interstitial thermotherapy (LITT) is a technique for the localized treatment of tumors wherein cancer cell necrosis is produced by moderate (noncharring) heating of the tumor with a laser source to temperatures above 43°C [1–4]. The lasers used for LITT are typically high power continuous-wave (CW), near-infrared lasers, such as the Nd:YAG laser (1064 nm), or different types of diode lasers (808–980 nm), which also have favorable tissue transmission characteristics [5,6]. The laser energy is generally delivered through optical fiber probes inserted into the body under X-ray, MRI, or ultrasonic guidance [7–9].

Ideally, the temperature rise produced within the treatment site using LITT must be controlled to avoid vaporization and carbonization, yet still ensure total tumor cell necrosis within the desired volume of treatment. In vital organs such as the liver, brain, or prostate, minimizing collateral thermal damage of healthy tissue surrounding the tumor is essential. Currently, one of the main limitations in the clinical application of laser hyperthermia is the lack of real-time intraoperative dosimetry of the laser-induced thermal effect [10].

Laser treatment parameters (such as power, duration, wavelength) and the resultant radiant field of the fiber for a given treatment procedure are initially selected by predicting the laser-induced temperature rise with tissue thermo-optical models of varying complexity [11–14]. However, because of tissue inhomogeneity, anisotropy, and variations of the optical and thermal properties of the tissues with temperature, thermo-optical models are not always sufficiently well parametrized to predict the temperature rise within the tissue with the desired accuracy or reliability. The suitability of the selected treatment parameters must, therefore, be demonstrated experimentally in tissue phantoms or in animal models. In situ interstitial temperatures generated during clinical or experimental laser irradiation are generally measured with thermocouple probes [15,16], infrared optical fibers [17,18], optical temperature sensors such as temperature-sensitive fluorescent probes [19,20], and MRI monitoring [21].

Thermocouple probes are more accurate and less expensive than fiber-optic or fluorescent temperature probes. However, they usually consist of thermocouple wires embedded in a thin needle made of stainless steel, which itself strongly absorbs near-IR radiation ~1,000 nm. Because this absorption induces a direct temperature increase of the needle, temperatures measured with thermocouple probes during laser irradiation of tissue may be significantly larger than the actual surrounding tissue temperature [22,23]. The amplitude of this artifact is usually assumed to be equal to the temperature jump recorded when the laser is switched on or off [22–24]. However, this correction technique does not provide an accurate quantification of the artifact because the endpoints of the jump usually cannot be identified accurately. In a variation of this technique [24], the laser was turned off for a short duration (1 s) at regular intervals during the treatment, and the artifact was assumed to be equal to the resulting temperature jumps. With this technique, the artifact is accurately quantified only if the laser is switched off longer than the time it takes for the thermocouples to reach thermal equilibrium with the surrounding tissue. If the laser is switched off for a shorter time, then the amplitude of the artifact is underestimated.

As part of the optimization of a procedure for stereotactic X-ray-guided LITT of small breast cancers [25,26], we have designed a system for in situ real-time temperature measurements during experimental LITT, using several needle thermocouple probes placed within the tissue around the LITT fiber probe [26–28]. The purpose of the present study was to quantify and subsequently correct for the artifact induced in temperature measurements made with thermocouples during LITT. This further enables us accurately to model the actual temperature increase in the treated tissue volume associated with a given set of laser treatment parameters.

MATERIALS AND METHODS

Laser and Fiber-Optic Probes

In all experiments, a CW Nd:YAG laser system (FiberTome™, Dornier Medical Systems, Germany) was set to a constant power output of 20W for 25–30 s. The laser energy was delivered through a silica fiber-optic probe, which consisted of a 600-μm core optical fiber terminated with a 200-mm-long quartz tip having an outer diameter of 1.9 mm (H-6190-1, Dornier Deutsche Aerospace, Germany). In the Dornier system, the axis of the LITT fiber is tilted by a small angle with respect to the optical axis of the laser beam and laser-to fiber coupling lens. With this design, the emission pattern at the fiber output is a diverging ring (Fig. 1). A quartz cap protects the fiber end

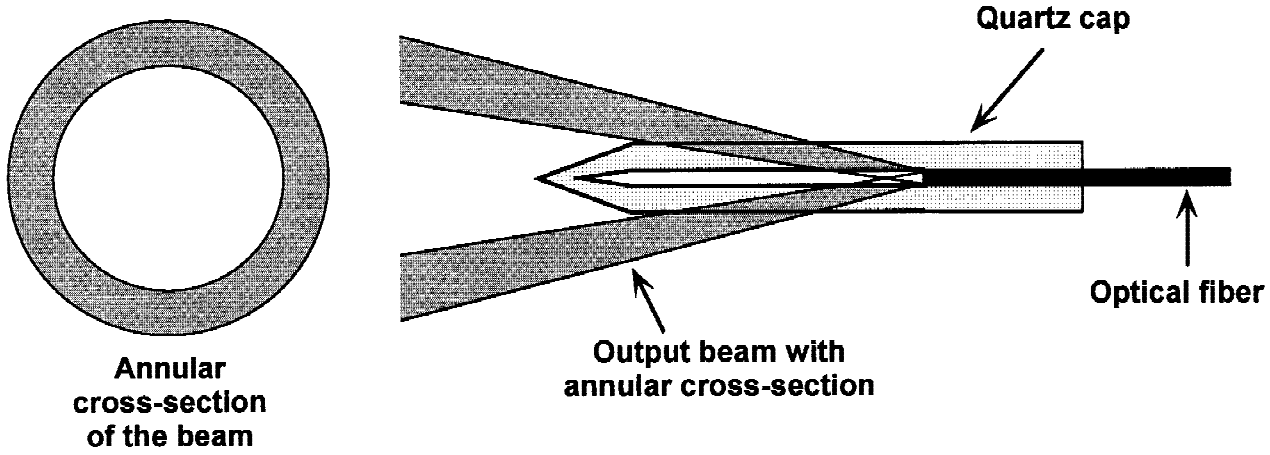

Fig. 1. Emission pattern at the output of the Dornier LITT probe in air.

face to ensure consistent light emission of the probe. The quartz cap increases the irradiated area at the output of the probe and thus helps reduce the temperature increase close to the tip to avoid charring. The power emitted by the LITT fiber probes was measured before and after each experiment by placing the output end of the fiber in an integrating sphere (UDT 2525, United Detector Technologies, Santa Monica, CA) through the input port and connecting a photodiode to the output port. The integrating sphere was initially calibrated at 1064 nm against a calibrated power meter (210, Coherent, Auburn, CA).

Temperature Measurements

Temperatures around the LITT probe were measured during laser irradiation in ambient air, water, 0.4% intralipid solution, and fatty cadaver porcine tissue with up to 15 separate 23-gauge (635 μm diameter), 5-cm-long, stainless-steel needle thermocouple probes with a time constant of 0.15s (MT-23/5, Physitemp Instruments, Clifton, NJ) held in position with a Plexiglas grid. The holes in the Plexiglas grid and weights added to the thermocouple probe helped avoid lateral and vertical movements of the probes during experiments. The thermocouples were connected to a 16 channel data acquisition system (DAS-TC, Omega Engineering, Stamford, CT), which allowed temperatures to be recorded every 0.3 s and displayed in real-time with a personal computer. One of the 16 channels of the data acquisition system was connected to an internal laser power signal to monitor and record the laser output power during the treatment cycle. After their individual calibration, temperatures recorded by each thermocouple were within 0.1°C of the temperatures measured against a calibrated precision thermometer in a water bath. The thermocouple needle probes had a manufacturer specified time constant of 0.15s and an operating range of –273–200°C.

Tissue Preparation

Fatty cadaver porcine tissue was obtained from the Division of Veterinary Resources, University of Miami. The skin, subcutaneous fat, and underlying muscle were obtained as a unit. Upon receipt, the tissues were sealed in plastic bags, and stored at 3°C for 2–6 weeks. Prior to testing, the tissue samples in sealed plastic bags were placed under flowing warm water until the core temperature was 35–37°C. The samples were then slightly compressed to prevent motion during fiber and thermocouple insertion and placed in the container of a temperature-controlled water bath that brought the initial tissue temperature to between 33–36°C.

Placement of Fiber and Thermocouple Probes

The LITT fiber was inserted laterally in the tissue through a port in the side of the water bath. To allow accurate positioning deep within the tissue while avoiding bending of the fiber, a guidance channel was first opened in the tissue with a 13-gauge stainless steel trocar-cannula assembly prior to fiber insertion. The trocar was then removed and the fiber was inserted in its place through the cannula. The cannula was then retracted so as to expose the quartz tip of the fiber.

The thermocouple probes were held in position above the water bath by a Plexiglass lid arrayed with holes spaced at 5 mm intervals for insertion of the thermocouples (Fig. 2). The verti-

cal position of each of the thermocouples was adjusted with depth stops so that all tips were brought to the same plane orthogonally to the lid and at the depth of the LITT fiber axis. To facilitate insertion of the thermocouple probes into the tissue, each insertion site was punctured beforehand with a 20-gauge hypodermic needle. The same technique for fiber and thermocouple placement was used in the experiments in the other media, except that the container was either left empty for the experiments in air, or filled with water or 0.4% intralipid solution.

RESULTS

Temperature Recordings

The observed temperature increase recorded for one of the thermocouples (TC5) in each of air, water, 0.4% intralipid solution, and porcine tissue is shown in Figure 3. The temperature of each of the 15 thermocouples in air varied exponentially with time. The temperature curves in air were fit with a function of the form:

$$\Delta T(t) = A\left(1 - e^{-\frac{t}{\tau}}\right) \qquad \text{(Eq. 1)}$$

where ΔT (in units of °C) is the temperature increase, A (in units of °C) is the asymptotic temperature, and τ (in units of s) is the time constant defined as the time to reach 63% of the asymptotic value. For irradiation in air, the asymptotic temperature reached up to 118.6°C for the thermocouple (TC15) subject to the most direct irradiation (Table 1, Fig. 3). The observed time constants for irradiation in air varied from 4.6–48 s (Table 1). Because air does not appreciably absorb near-infrared radiation, these temperature increases were the result of direct light absorption by the thermocouple probes themselves. Since the emission pattern of the LITT probe in air was a forwardly diverging annulus, only the thermocouple probes placed directly in the light cone underwent a significant temperature increase. As shown in Table 1, the thermocouple placed immediately in front of the probe (TC15) was located in a region of higher radiance in this medium than the other thermocouples, whose observed temperature rises were all <5% that of TC15. These thermocouples were located outside the main emission field of the LITT probe. The higher temperature increase of TC15 also indicates that a significant amount

TABLE 1. Coefficients of the curve fits*

	Air				Water				Intralipid				Ex vivo porcine fat			
TC#	A (°C)	τ (s)	B (°C/s)	r^2	A (°C)	τ (s)	B (°C/s)	r^2	A (°C)	τ (s)	B (°C/s)	r^2	A (°C)	τ (s)	B (°C/s)	r^2
15	118.6	4.6	0	1.000	2.2	3.2	0.10	0.988	0.7	7.0	0.04	0.968	2.1	1.5	0.14	0.994
14	3.3	24.4	0	0.979	—	—	—	—	2.0	7.6	0.00	0.965	1.1	1.5	0.07	0.974
13	3.1	20.1	0	0.977	—	—	—	—	1.6	5.3	0.02	0.967	1.3	1.2	0.10	0.988
12	3.8	27.1	0	0.983	—	—	—	—	4.7	1.8	0.04	0.987	6.2	1.8	0.30	0.998
11	4.7	26.3	0	0.990	—	—	—	—	2.7	1.6	0.03	0.980	6.5	1.4	0.44	0.999
10	3.1	28.0	0	0.978	—	—	—	—	1.9	2.2	0.03	0.963	4.8	1.8	0.23	0.998
9	4.5	48.0	0	0.977	—	—	—	—	1.3	3.4	0.03	0.956	4.2	1.4	0.33	0.999
8	3.6	8.0	0	0.992	—	—	—	—	—	—	—	—	1.3	1.8	0.06	0.975
7	3.4	10.0	0	0.989	—	—	—	—	—	—	—	—	1.1	1.6	0.08	0.980
6	4.5	11.2	0	0.991	8.1	1.2	0.05	0.993	6.3	0.8	0.00	0.988	17.9	2.2	0.71	0.998
5	6.5	9.6	0	0.996	9.9	1.0	0.06	0.992	3.3	1.5	0.02	0.983	13.8	1.9	0.88	1.000
4	3.9	9.0	0	0.992	6.1	1.5	0.03	0.994	—	—	—	—	1.5	2.2	0.09	0.988
3	4.0	9.0	0	0.991	6.8	1.2	0.04	0.994	—	—	—	—	1.8	1.4	0.14	0.994
2	1.9	8.9	0	0.968	—	—	—	—	—	—	—	—	1.1	3.0	0.03	0.948
1	1.8	13.2	0	0.967	—	—	—	—	—	—	—	—	0.3	2.3	0.05	0.944

*The thermocouples in water and intralipid whose parameters are not listed in the table did not undergo a detectable temperature increase due to direct absorption of light. A, Asymptotic temperature; τ, Time constant; B, slope; r^2, Correlation coefficient.

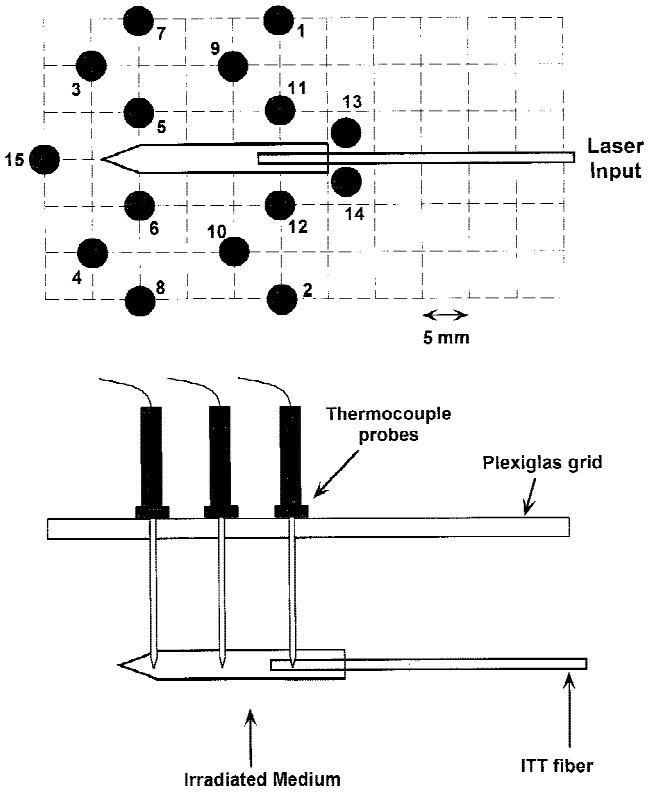

Fig. 2. Position of the 15 thermocouples around the LITT fiber. The tip of each thermocouple was located in the plane perpendicular to the thermocouples and containing the axis of the fiber probe.

of light is emitted in the forward direction outside the main emission ring.

To analyze the temperatures recorded in water, intralipid, and porcine tissue, we assumed that the recorded temperature increase was the sum of two terms: the temperature increase due to light absorption in the medium and the temperature increase due to direct absorption of light by the thermocouple (Eq. 1). Because the estimated thermal relaxation times of water, 0.4% intralipid solution and porcine fatty tissue at 1,064 nm (e.g. >1,800s for water, calculated at 1,064 nm) are so much longer than the irradiation time (30 s) of these experiments, the resulting temperature increase in the tissue, $\Delta T(r,t)$, was expected to vary linearly with time under constant power input [29]:

$$\Delta T(r,t) = \frac{\mu_a}{\rho\, c} F(r)\, t \qquad \text{(Eq. 2)}$$

where μ_a (in units of cm^{-1}) is the absorption coefficient at 1,064 nm, ρ (in units of $g.cm^{-3}$ is the density, c (in units of $J.g^{-1}.°C^{-1}$) is the heat capacity, and F(r) (in units of W/cm^2) is the fluence rate. Accordingly, the temperature curves measured in water, intralipid solution and porcine tissue were fit with functions of the form:

$$\Delta T(t) = A\left(1 - e^{-\frac{t}{\tau}}\right) + Bt \qquad \text{(Eq. 3)}$$

where the exponential term represents the temperature increase due to direct absorption of light by the thermocouple, and B ($°C.s^{-1}$) is the slope of the linear temperature increase due to absorption of light by the medium. The fitted values of A, τ and B for all thermocouples in water, intralipid and porcine tissue experiments are shown in Table 1.

In water as in air, only those thermocouples located in regions of direct laser radiance underwent significant temperature increase. Other thermocouples, not shown in Table 1, experienced temperature increases of <3°C, with variable delays of 6–12 s after the laser irradiation was commenced. These thermocouples were heated by advection. In intralipid solution, the thermocouples located farthest from the probe (TC 1, 2, 3, 4, 7, 8) recorded temperature increases of <2°C, again with initial delays of up to 5 s. The fluence rate at these locations was probably not sufficient to induce a measurable temperature increase due to light absorption either by the thermocouple needles or by the immediately surrounding intralipid itself. These thermocouples were also probably heated by advective process.

Removal of Thermocouple Artifact in Pig Tissue

The artifact due to light absorption by the thermocouples was simply removed from the measurements in porcine tissue by subtracting the exponential term in Eq. (3) from the measured temperature increases (Fig. 4). This correction was made for each thermocouple by using the corresponding values of A and τ listed in Table 1. For times greater than 4.6 (2 × e) times the time constant τ, the value of the exponential term is within 1% of the asymptotic value, so that the artifact for these times was effectively equal to the asymptotic value, A, of the exponential term. In porcine tissue, the magnitude of the direct absorption artifact varied from 0.3–17.9°C depending upon the placement of the thermocouple in the tissue light field.

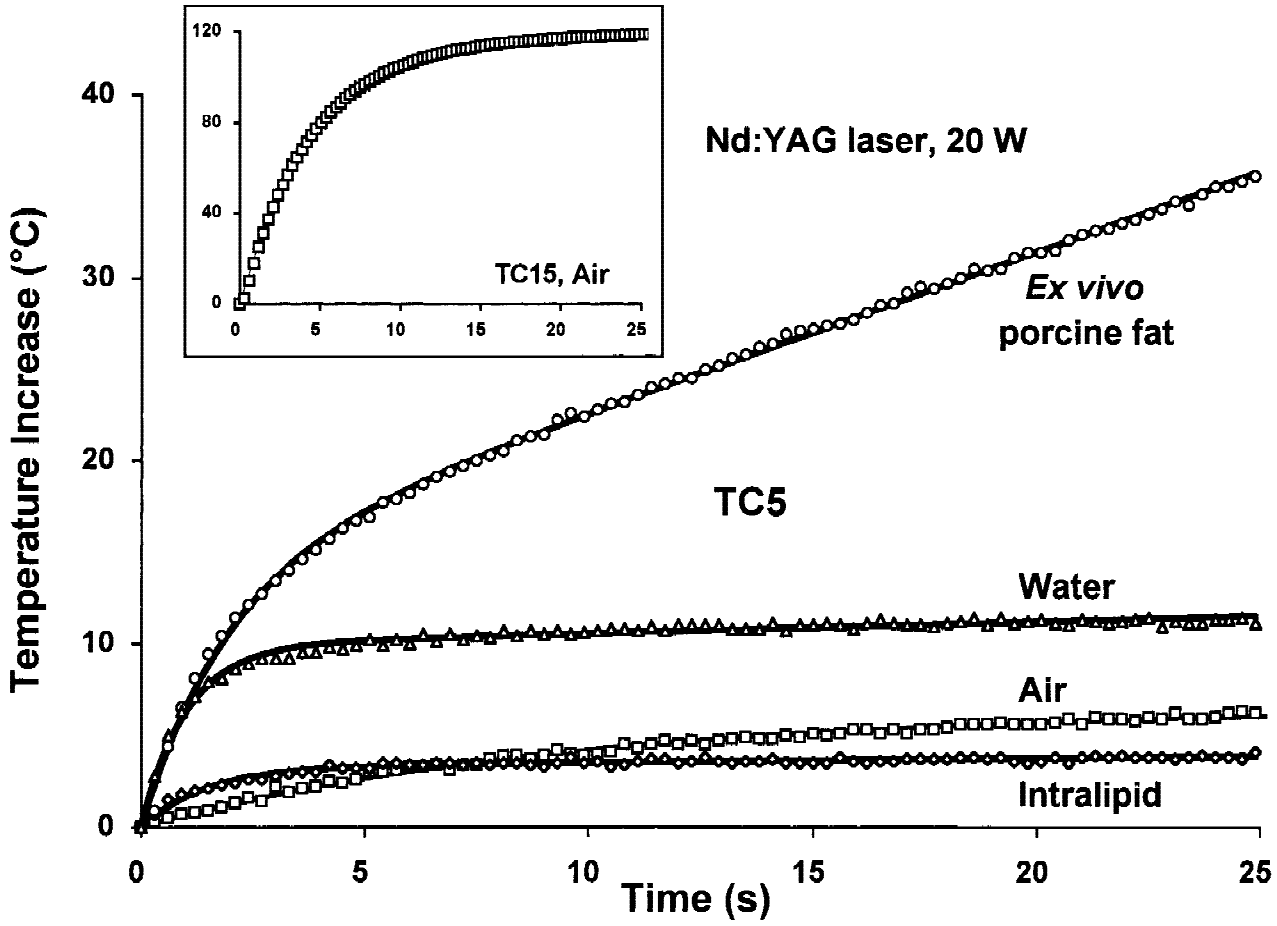

Fig. 3. Temperature increase recorded by the thermocouple at grid position 5 (TC5) in air, water, 0.4% intralipid solution, and porcine fat during Nd:YAG laser irradiation at 20W. Insert shows the temperature increase of thermocouple 15 (TC15) in air. Plotted symbols represent the measured temperature points. Solid lines are calculated curve fits.

DISCUSSION

Effect of Thermocouple

The experiments in air demonstrated that the temperature increase due to direct absorption of light by the thermocouple probes varied exponentially with time. These variations can be explained by using a heat conduction model wherein the thermocouple probe is considered to be a thin solid cylinder of thermal conductivity much higher than air heated by a constant heat source and immersed in a medium maintained at uniform temperature. Such a system can be analyzed by using a "lumped system formulation" where the variation of temperature within the thermocouple probe is neglected due to its higher thermal conductivity [30]. One can show that the solution of such a transient heat conduction problem with heat generation yields an exponential function of the form of Eq. (1), wherein the asymptotic value, A, represents the temperature at thermal equilibrium, and the time constant, τ, is representative of the time needed to reach thermal equilibrium.

In porcine tissue, a highly scattering medium, the time constant of the exponential function representing the temperature increase due to light absorption by the thermocouple probes varied between 1.2–3.0 s depending on the exact spatial location of the thermocouple in the measurement grid pattern. The temperature change due to light absorption by the tissue during the time taken for the thermocouple probes to reach thermal equilibrium (defined as 2.3 times the time constant τ of the exponential temperature increase, which is the time to reach 90% of the asymptotic value of the exponential term), was calculated for each thermocouple by using the corresponding values of B (Table 1). This temperature change varied between 0.2–3.6°C. Thus the tem-

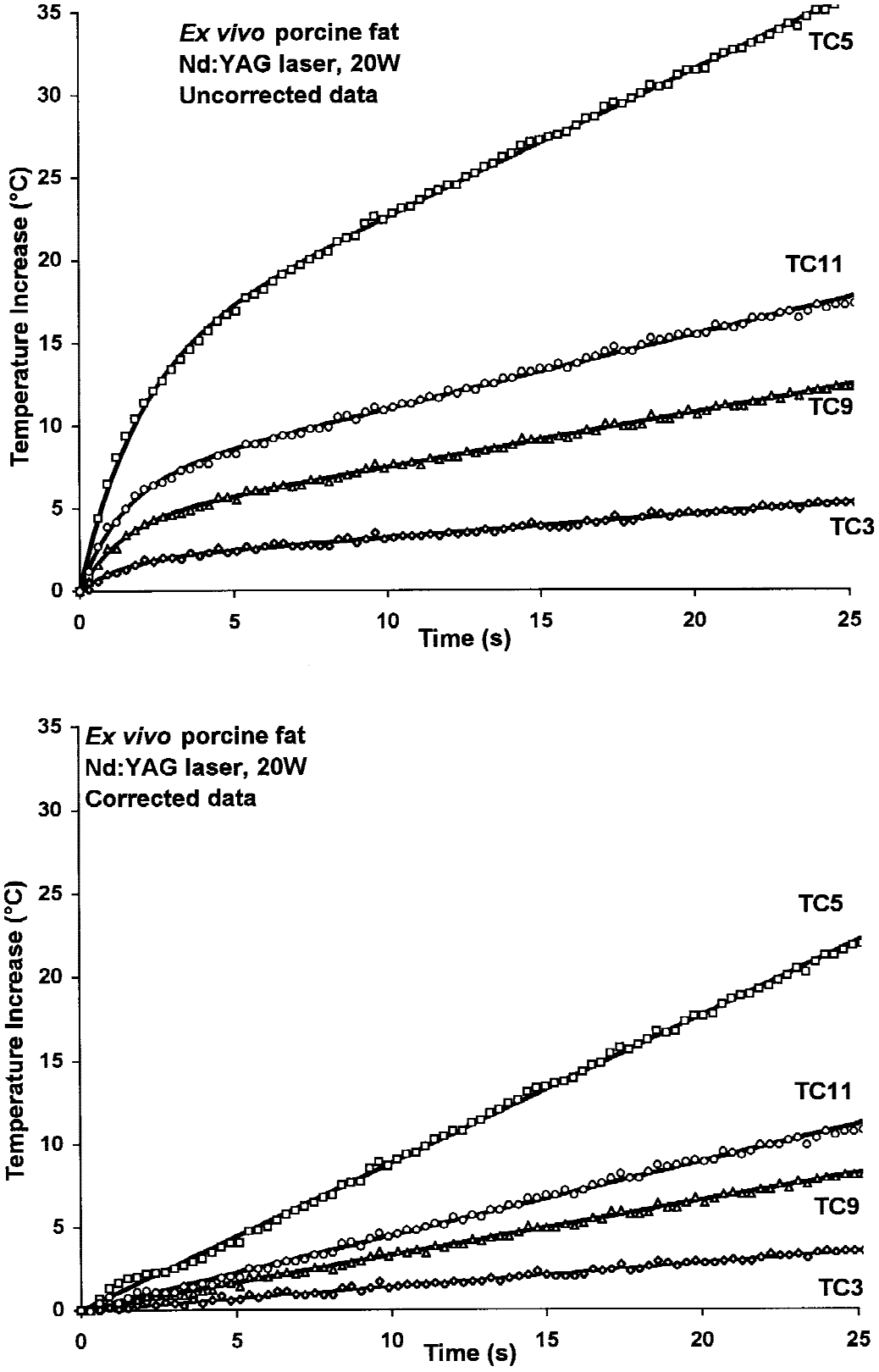

Fig. 4. Temperature increase of four thermocouples in porcine fat during Nd:YAG laser irradiation at 20W before and after removal of the thermocouple artifact. Plotted symbols represent the measured temperatures. Solid lines are the calculated curve fits.

perature of the medium surrounding the thermocouple probe can be assumed to be constant during the time taken for the thermocouple to reach thermal equilibrium. The lumped system analysis, therefore, can also be applied for porcine fatty tissue and any other biological tissue exhibiting comparable absorption and scattering characteristics towards near-IR radiation.

Removal of Thermocouple Artifact

In order to be able accurately to predict the dosimetry of an applied laser fluence rate in a given tissue, it is first necessary to remove any thermocouple artifact from the recorded temperature field. The thermocouple artifact was simply removed from the porcine tissue data by subtracting the exponential term of the fitted curve from the measured data. This correction is possible only if the time constant of the exponential term is much smaller than the thermal relaxation time of the tissue. Additionally, the temperature increase due to light absorption by the thermocouple probes can be fit accurately only if the temperature is measured at a rate sufficiently high to provide enough data points to characterize the exponential rise. In porcine tissue, having time constants ranging from 1.2–3.0 s, the temperature must be measured at least every 0.5 s. However, even with slower data acquisition rates, the recorded data still can be corrected for times larger than 4.6 times the time constant (time to reach 99% of the asymptotic value of the exponential function), by taking the intercept on the ordinate axis of the linear part of the temperature curve. The temperature at the ordinate intercept corresponds to the asymptotic value of the exponential function, A, which is the thermocouple artifact.

An alternate analysis of the observed temperature decrease immediately after the laser is turned off should also provide a means of accounting for the thermocouple artifact discussed here. Further analysis of the laser-induced temperature rise in our tissue model will be the subject of additional publications.

Other Possible Artifacts Due to Presence of Thermocouple Probes

Typically, thermocouple probes are only partially immersed in the test medium for temperature measurements, leaving the proximal end and the shaft of the stainless steel probes exposed to air at room temperature. Because of their high thermal conductivity, the thermocouple probes act as heat sinks, and a temperature gradient is thus formed along the probes and in the surrounding tissue when thermal equilibrium is reached in the absence of laser radiation. Heating of the thermocouple probes by direct light absorption induces an additional temperature gradient in the medium nearby the thermocouple probe. For these reasons, the temperatures obtained after removal of the artifact due to direct light absorption by the thermocouples may still not be the true tissue temperatures. Ideally, the tissue temperature can be measured without artifact only if the thermocouple probes have the same thermal and optical properties as the surrounding medium [31].

The temperature gradients induced by the presence of the thermocouples may be a significant source of measurement error in the absolute recorded temperature, $T(r,t)$, but most likely not in the relative temperature increase, $\Delta T(r,t)$. According to the simple model of Eq. (2), when the irradiation time is much shorter than the thermal relaxation time of the tissue, the temperature increase due to light absorption in the tissue is independent of the initial temperature distribution. In other words, the temperature gradient caused by each thermocouple probe after it reaches thermal equilibrium does not substantially affect the subsequent change in tissue temperature due to light absorption in the tissue. It is only when heat diffusion becomes significant, i.e., when the irradiation time is on the order of the thermal relaxation time, that the temperature gradients due to the thermocouples also may induce a significant error in the calculated temperature increases. Finally, it may be noted that the absorption properties of the thermocouples may themselves be a function of the laser irradiation wavelength, so that the magnitude of any thermocouple error may change with the use of different laser radiation sources.

CONCLUSIONS

Our experiments demonstrate that absorption of laser radiation by stainless steel thermocouple probes may induce a significant overestimation of the temperature measured during laser irradiation of tissue. When the time constant of the thermocouple effect is much smaller than the thermal relaxation time of the surrounding tissue, the artifact can be clearly and accurately quantified and if need be, corrected for. In LITT, where differences of a few degrees in temperature are significant to the desired therapeutic out-

come, correction of experimentally recorded thermocouple measurements is necessary in order to be able to predict the treatment effect and accurately to model experimentally recorded temperature fields.

ACKNOWLEDGMENTS

We thank Dornier USA for the loan of the Nd:YAG laser.

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